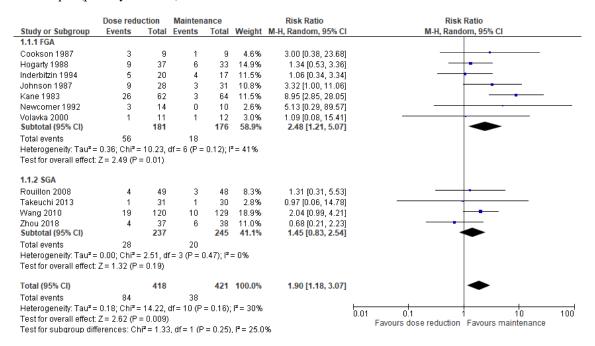
# Supplementary Figure S7. Forest plot: Subgroup analysis, factors related to antipsychotic use and dose reduction strategy

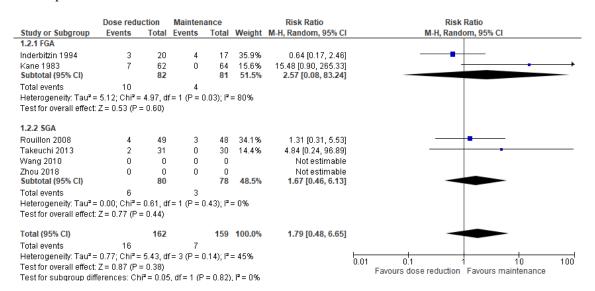
#### A. Antipsychotics: type

#### 1. Relapse/Hospitalization

#### 1.1 Relapse (primary outcome)

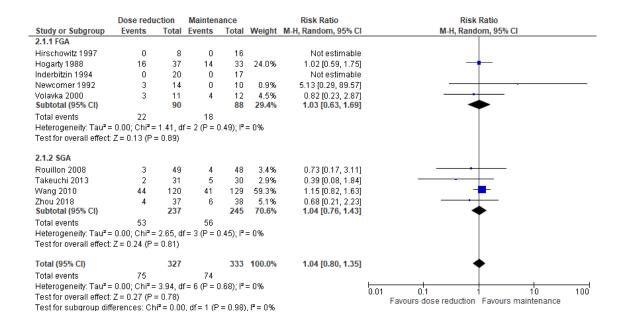


### 1.2 Hospitalization

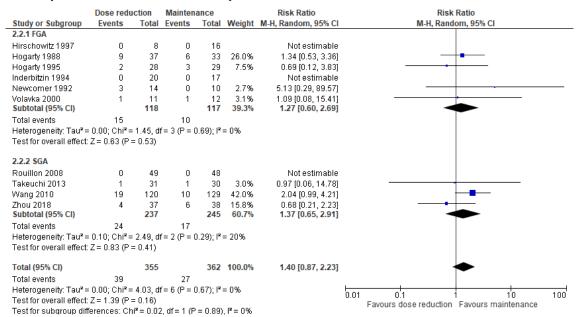


#### 2. Study discontinuation

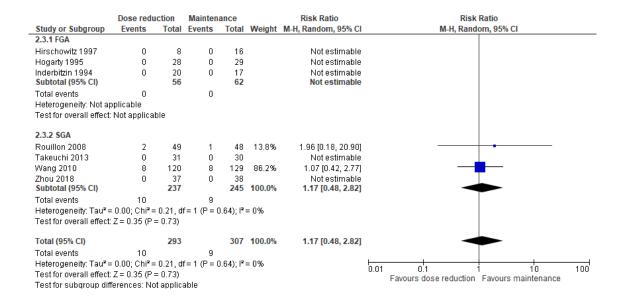
#### 2.1 Study discontinuation due to all causes



#### 2.2 Study discontinuation due to inefficacy

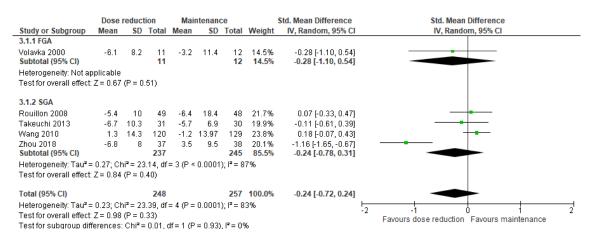


# 2.3 Study discontinuation due to intolerability

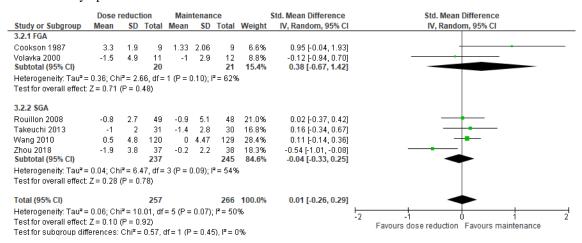


#### 3. Psychopathology

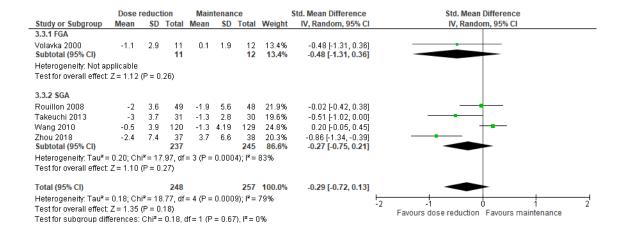
#### 3.1 Total



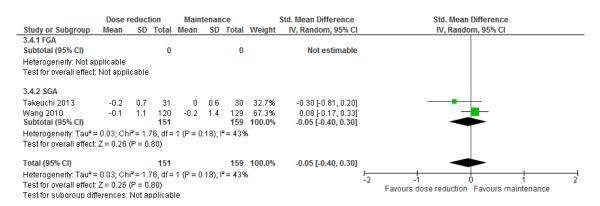
#### 3.2 Positive symptoms



# 3.3 Negative symptoms

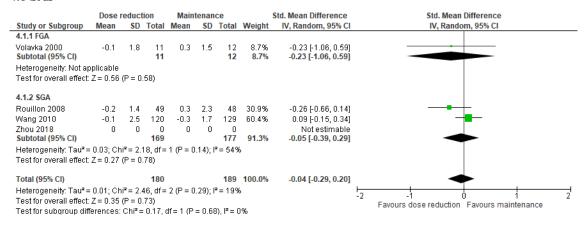


#### 3.4 CGI-S

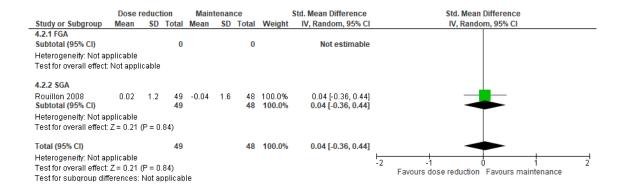


#### 4. Adverse effects

#### 4.1 SAS



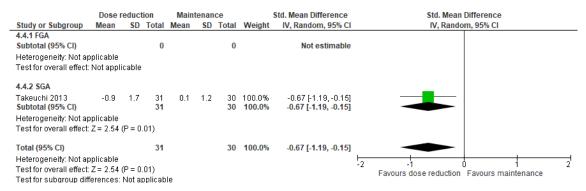
#### **4.2 BARS**



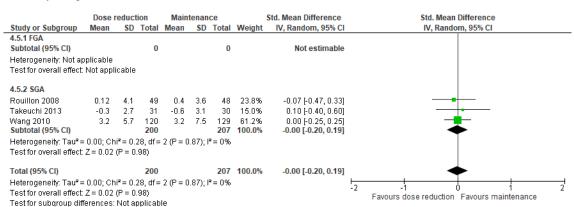
#### **4.3 AIMS**

	Dose	reduct	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.3.1 FGA									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Not appl	icable							
4.3.2 SGA									
Rouillon 2008	-0.1	1.6	49	-0.4	1.7	48	100.0%	0.18 [-0.22, 0.58]	<del></del>
Subtotal (95% CI)			49			48	100.0%	0.18 [-0.22, 0.58]	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z= 0.89	(P = 0.	.38)						
Total (95% CI)			49			48	100.0%	0.18 [-0.22, 0.58]	-
Heterogeneity: Not ap	plicable								-2 -1 0 1
Test for overall effect:	Z = 0.89	(P = 0.	.38)						-2 -1 U 1 Favours dose reduction Favours maintenance
Test for subaroup diff	ferences:	Not as	nnlicah	le					Favours dose reduction Favours maintenance

# 4.4 DIEPSS



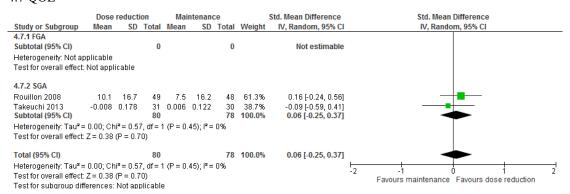
# 4.5 Body weight



# 4.6 Neurocognition

	Dose	reduct	ion	Mair	itenan	ce		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI
4.6.1 FGA										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not ap	oplicable									
Test for overall effect:	Not app	licable								
4.6.2 SGA										
Takeuchi 2013	7	7.1	31	-0.1	8	30	45.4%	0.93 [0.40, 1.46]		
Zhou 2018	9.8	13.7	37	3.6	11.5	38	54.6%	0.49 [0.03, 0.95]		
Subtotal (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]		
Heterogeneity: Tau² =	= 0.03; CI	$hi^2 = 1.9$	52, df=	1 (P = I	0.22); I	<sup>2</sup> = 349	ó			
Test for overall effect:	Z = 3.12	(P = 0	.002)							
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]		-
Heterogeneity: Tau <sup>2</sup> =	0.03; CI	hi² = 1.9	52, df=	1 (P = I	0.22); [	<sup>2</sup> = 349	6		-2	<del></del>
Test for overall effect:	Z = 3.12	(P = 0	.002)						-2	Favours maintenance Favours dose reduction
Test for subgroup diff	ferences	: Not a	oplicab	le						Tavours maintenance Tavours dose reduction

# 4.7 QOL

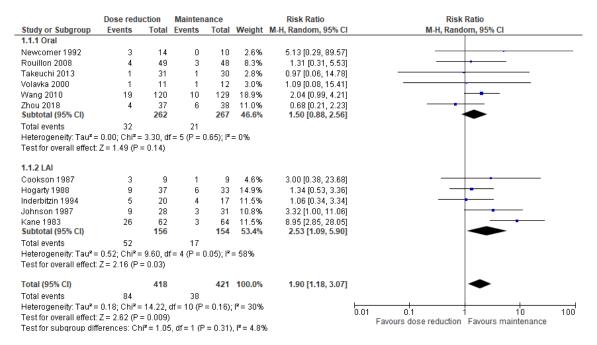


Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; FGAs, first-generation antipsychotics; QOL, quality of life; SAS, Simpson-Angus Scale; SGAs, second-generation antipsychotics

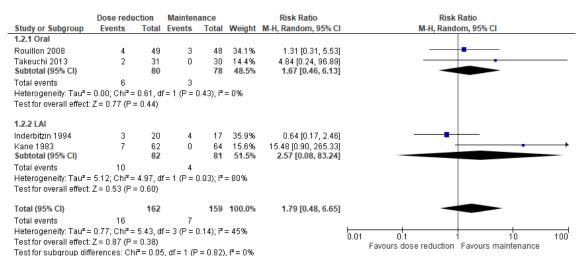
# B. Antipsychotic: formulation

#### 1. Relapse/Hospitalization

#### 1.1 Relapse (primary outcome)

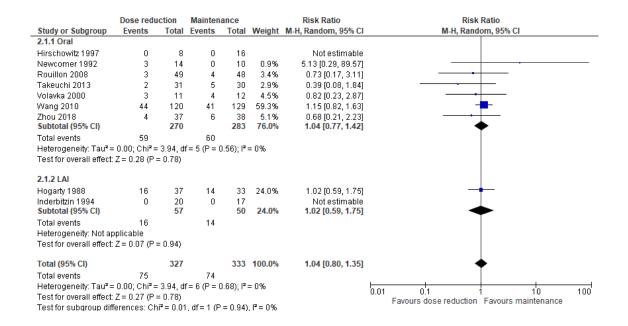


# 1.2 Hospitalization

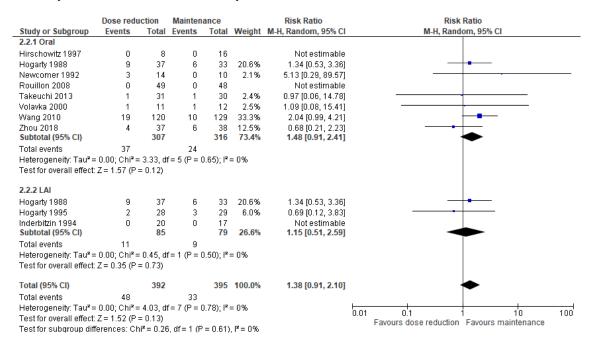


# 2. Study discontinuation

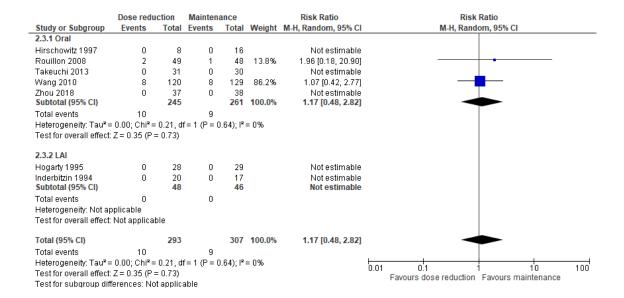
# 2.1 Study discontinuation due to all causes



# 2.2 Study discontinuation due to inefficacy

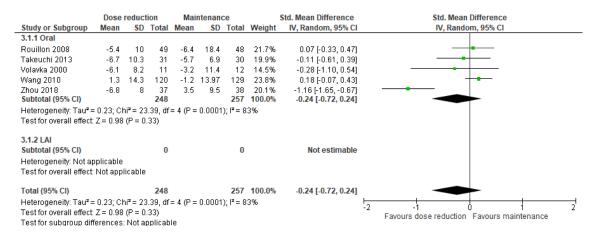


# 2.3 Study discontinuation due to intolerability

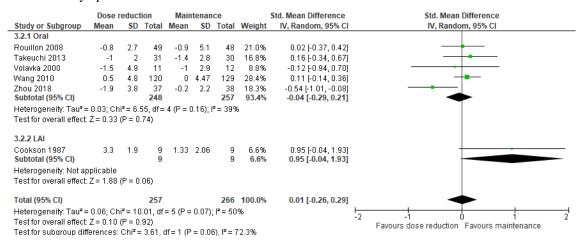


#### 3. Psychopathology

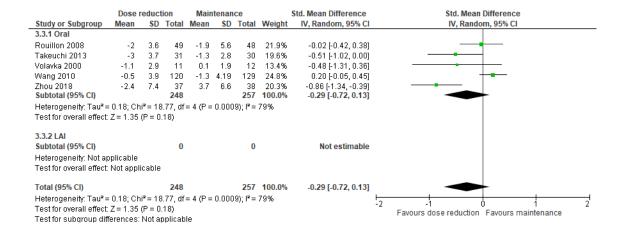
#### 3.1 Total



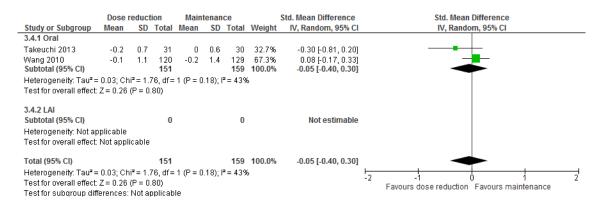
#### 3.2 Positive symptoms



# 3.3 Negative symptoms

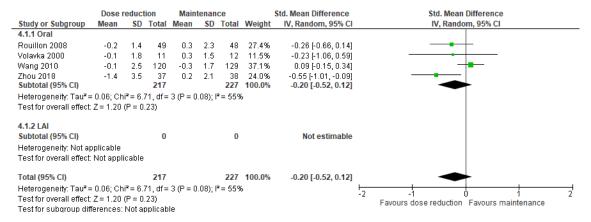


#### 3.4 CGI-S



#### 4. Adverse effects

#### 4.1 SAS



#### **4.2 BARS**

	Dose r	educti	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.2.1 Oral									<u></u>
Rouillon 2008 Subtotal (95% CI)	0.02	1.2	49 <b>49</b>	-0.04	1.6	48 <b>48</b>	100.0% <b>100.0%</b>	0.04 [-0.36, 0.44] <b>0.04 [-0.36, 0.44]</b>	-
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 0.21 (	P = 0.	84)						
4.2.2 LAI									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Not appli	cable							
Total (95% CI)			49			48	100.0%	0.04 [-0.36, 0.44]	-
Heterogeneity: Not ap	plicable								-2 -1 0 1 2
Test for overall effect:	Z = 0.21 (	P = 0.	84)						Favours dose reduction Favours maintenance
Test for subgroup diff	ferences:	Not ap	plicab	le					r avours dose reduction. Favours maintenance

# **4.3 AIMS**

	Dose r	educt	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
4.3.1 Oral										
Rouillon 2008 Subtotal (95% CI)	-0.1	1.6	49 <b>49</b>	-0.4	1.7	48 <b>48</b>	100.0% <b>100.0%</b>	0.18 [-0.22, 0.58] <b>0.18 [-0.22, 0.58]</b>		
Heterogeneity: Not app	licable									
Test for overall effect: Z	= 0.89 (	(P = 0.	38)							
4.3.2 LAI										
Subtotal (95% CI)			0			0		Not estimable	•	
Heterogeneity: Not app	licable									
Test for overall effect: N	lot appli	cable								
Total (95% CI)			49			48	100.0%	0.18 [-0.22, 0.58]	-	
Heterogeneity: Not app	licable									ᆜ
Test for overall effect: Z	= 0.89 (	(P = 0.	38)						-2 -1 0 1 Favours dose reduction Favours maintenance	- 2
Test for subgroup differ	rences:	Not ap	plicab	le					ravours dose reduction Favours maintenance	

# 4.4 DIEPSS

	Dose r	reduct	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.4.1 Oral									
Takeuchi 2013 Subtotal (95% CI)	-0.9	1.7	31 <b>31</b>	0.1	1.2	30 <b>30</b>	100.0% <b>100.0%</b>	-0.67 [-1.19, -0.15] - <b>0.67 [-1.19, -0.15]</b>	
Heterogeneity: Not as	oplicable								
Test for overall effect:	Z = 2.54	(P = 0	.01)						
4.4.2 LAI Subtotal (95% CI) Heterogeneity: Not ap	onlicable		0			0		Not estimable	
Test for overall effect:		icable							
Total (95% CI) Heterogeneity: Not ap Test for overall effect: Test for subgroup dif	Z= 2.54	•	,	ile		30	100.0%	-0.67 [-1.19, -0.15]	-2 -1 0 1 2 Favours dose reduction Favours maintenance

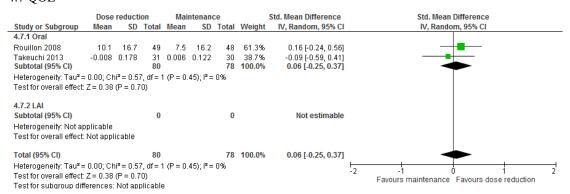
# 4.5 Body weight

	Dose i	reduct	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD						IV, Random, 95% CI	
4.5.1 Oral									
Rouillon 2008	0.12	4.1	49	0.4	3.6	48	23.8%	-0.07 [-0.47, 0.33]	] <del>- •</del>
Takeuchi 2013	-0.3	2.7	31	-0.6	3.1	30	15.0%	0.10 [-0.40, 0.60]	- <del>-  -</del>
Wang 2010 Subtotal (95% CI)	3.2	5.7	120 <b>200</b>	3.2	7.5	129 <b>207</b>	61.2% <b>100.0%</b>	0.00 [-0.25, 0.25] - <b>0.00 [-0.20, 0.19]</b>	
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:  4.5.2 LAI				2 (P = L	1.07), 1	= 0%			
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not as									
Test for overall effect:	Not appl	icable							
Total (95% CI)			200			207	100.0%	-0.00 [-0.20, 0.19]	•
Heterogeneity: Tau <sup>2</sup> = Test for overall effect: Test for subgroup diff	Z = 0.02	(P = 0.	.98)	•	l.87); I	= 0%			-2 -1 0 1 2 Favours dose reduction Favours maintenance

# 4.6 Neurocognition

	Dose	reduct	ion	Mair	itenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.6.1 Oral									
Takeuchi 2013	7	7.1	31	-0.1	8	30	45.4%	0.93 [0.40, 1.46]	
Zhou 2018	9.8	13.7	37	3.6	11.5	38	54.6%	0.49 [0.03, 0.95]	
Subtotal (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	
Heterogeneity: Tau <sup>2</sup> :	= 0.03; CI	ni² = 1.5	52, df=	1 (P = I	0.22); [	<sup>2</sup> = 349	6		
Test for overall effect	t: Z = 3.12	(P = 0	.002)	•					
4.6.2 LAI									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not a	pplicable								
Test for overall effect	: Not app	licable							
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	-
Heterogeneity: Tau <sup>2</sup> :	= 0.03; CI	ni² = 1.5	52. df=	1 (P = I	0.22); [	<sup>2</sup> = 349	6		
Test for overall effect				,	- ''				-2 -1 0 1 2
Test for subgroup dit		*		ile					Favours maintenance Favours dose reduction

# 4.7 QOL

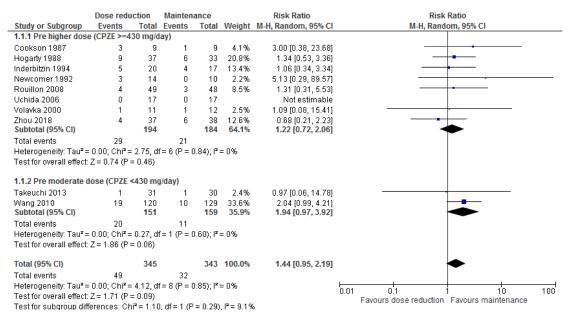


Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; LAI, long-acting injectable; QOL, quality of life; SAS, Simpson-Angus Scale

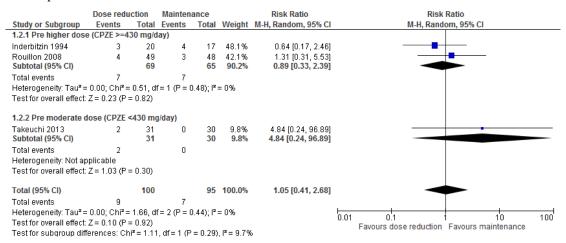
# C. Antipsychotics: mean dose before reduction

#### 1. Relapse/Hospitalization

#### 1.1 Relapse (primary outcome)

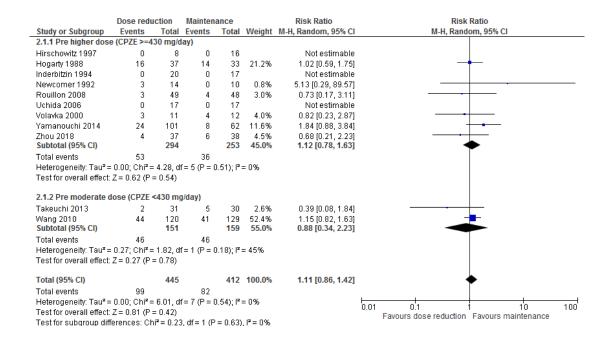


# 1.2 Hospitalization

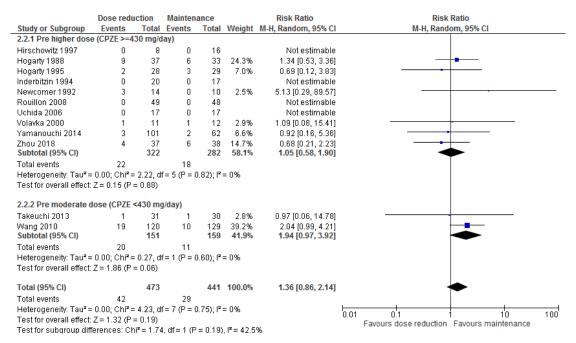


# 2. Study discontinuation

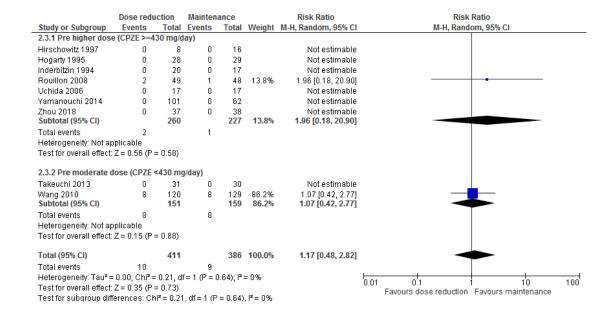
# 2.1 Study discontinuation due to all causes



#### 2.2 Study discontinuation due to inefficacy

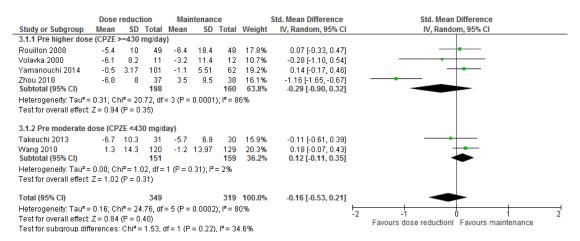


#### 2.3 Study discontinuation due to intolerability

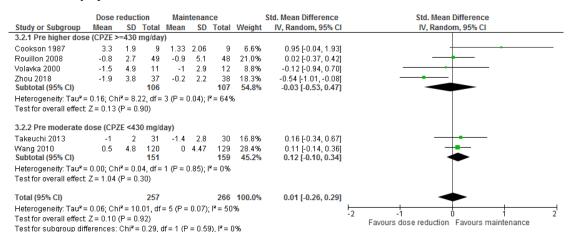


# 3. Psychopathology

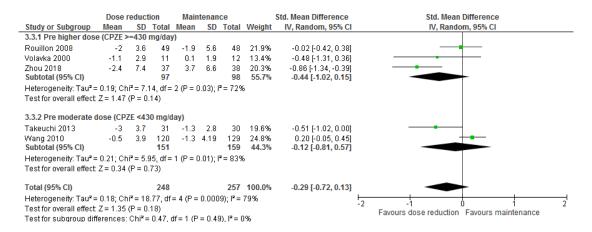
#### 3.1 Total



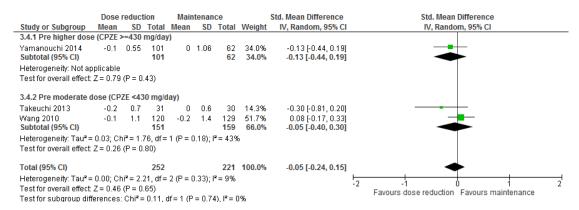
#### 3.2 Positive symptoms



# 3.3 Negative symptoms

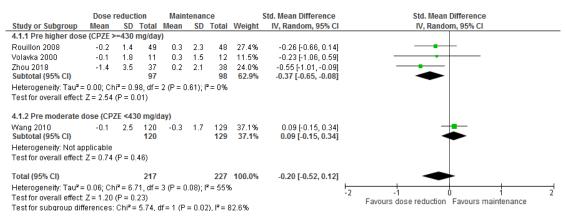


#### 3.4 CGI-S



#### 4. Adverse effects

#### 4.1 SAS



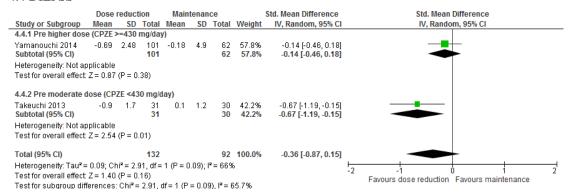
#### **4.2 BARS**

	Dose r	eduction	n N	laintena	nce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD To	otal Me	an SE	) Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.2.1 Pre higher dos	e (CPZE >	=430 mg	ı/day)					
Rouillon 2008 Subtotal (95% CI)	0.02	1.2	49 -0. <b>49</b>	.04 1.6	48 48		0.04 [-0.36, 0.44] <b>0.04 [-0.36, 0.44]</b>	-
Heterogeneity: Not a	pplicable							
Test for overall effect	Z = 0.21	(P = 0.84	)					
4.2.2 Pre moderate	dose (CPZ	ZE <430 r	ng/day)					
Subtotal (95% CI)			0		0		Not estimable	
Heterogeneity: Not a	pplicable							
Test for overall effect	: Not appli	icable						
Total (95% CI)			49		48	100.0%	0.04 [-0.36, 0.44]	
Heterogeneity: Not a	pplicable							
Test for overall effect	: Z = 0.21 /	(P = 0.84)	)					-2 -1 0 1 2 Favours dose reduction Favours maintenance
Test for subgroup dif	ferences:	Not anni	icable					ravours dose reduction - Favours maintenance

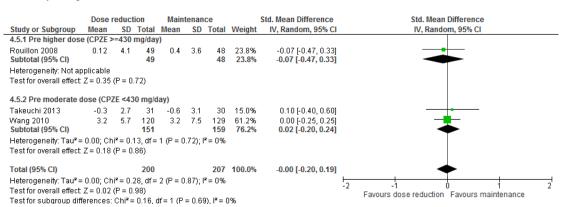
#### **4.3 AIMS**

	Dose re	educt	ion	Mair	ntenan	ice		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.3.1 Pre higher dos	e (CPZE >:	=430 ı	mg/day	)					
Rouillon 2008 Subtotal (95% CI)	-0.1	1.6	49 <b>49</b>	-0.4	1.7	48 <b>48</b>	100.0% <b>100.0%</b>	0.18 [-0.22, 0.58] <b>0.18 [-0.22, 0.58]</b>	
Heterogeneity: Not as	oplicable								
Test for overall effect:	Z = 0.89 (	P = 0.	38)						
4.3.2 Pre moderate of	dose (CPZ	E <43	0 mg/d	ay)					
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not as	oplicable								
Test for overall effect:	Not appli	cable							
Total (95% CI)			49			48	100.0%	0.18 [-0.22, 0.58]	
Heterogeneity: Not as	oplicable								-2 -1 0 1 2
Test for overall effect: Test for subgroup dif	,	•		e					Favours dose reduction Favours maintenance

# 4.4 DIEPSS



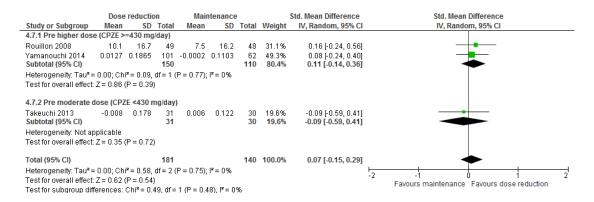
# 4.5 Body weight



# 4.6 Neurocognition

	Dose	reduct	ion	Mair	itenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.6.1 Pre higher dos	e (CPZE	>=430	mg/day	()					
Zhou 2018 Subtotal (95% CI)	9.8	13.7	37 <b>37</b>	3.6	11.5	38 <b>38</b>	54.6% <b>54.6%</b>	0.49 [0.03, 0.95] <b>0.49 [0.03, 0.95]</b>	
Heterogeneity: Not ap	oplicable								
Test for overall effect	Z = 2.07	(P = 0	.04)						
4.6.2 Pre moderate	dose (CP	ZE <43	80 mg/c	lay)					
Takeuchi 2013 Subtotal (95% CI)	7	7.1	31 <b>31</b>	-0.1	8	30 <b>30</b>	45.4% <b>45.4</b> %	0.93 [0.40, 1.46] <b>0.93 [0.40, 1.46]</b>	
Heterogeneity: Not as	oplicable								
Test for overall effect	Z= 3.43	(P = 0	.0006)						
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.03; CI	hi² = 1.:	52, df=	1 (P = I	0.22); I	<sup>2</sup> = 349	6		-2 -1 1
Test for overall effect				•	- ''				-2 -1 U 1 Favours maintenance Favours dose reduction
Test for subgroup dif	ferences	: Chi²=	: 1.52. (	df = 1 (F	= 0.23	2), $I^2 = 0$	34.4%		ravours maintenance Favours dose reduction

# 4.7 QOL



Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; CPZE, chlorpromazine equivalent; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; QOL, quality of life; SAS, Simpson-Angus Scale